Patient safety in the Eluvia DES and Ranger DCB programmes

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Disclosure

Speaker name:

William Gray

I have the following potential conflicts of interest to report:

- [x] Consulting (Boston Scientific)
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest

Boston Scientific Sponsored Studies of Paclitaxel-Eluting Devices

Device	Clinical Study	Design	Study Status
Eluvia™ Drug-Eluting Stent Paclitaxel dose: 0.167µg/mm²	MAJESTIC	Single-arm	3-year follow up, study complete
	IMPERIAL	Randomized	1-year follow up complete, ongoing to 5 years
	EMINENT	Randomized	Enrolling
	REGAL	Single-arm	Enrolling
Ranger™ Paclitaxel-Coated PTA Balloon Catheter Paclitaxel dose: 2 µg/mm²	RANGER SFA*	Randomized	3-year follow up 2019
	RANGER II	Randomized	1-year follow up 2019, ongoing to 5 years
SAVAL™ Drug-Eluting Stent Paclitaxel dose: 0.236 µg/mm²	SAVAL	Randomized & Single-arm phases	Enrolling

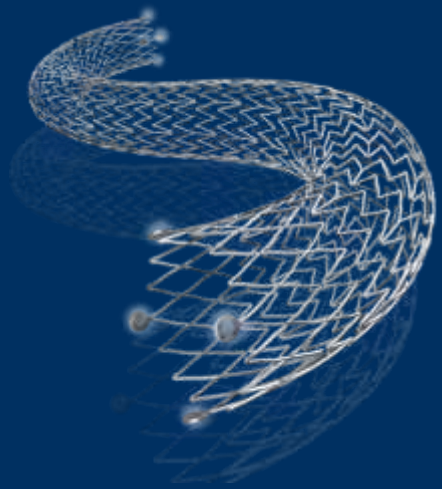
*RANGER SFA is sponsored by Hemoteq (a member of the Freudenberg Medical Group). Additional funding for data analysis was provided by Boston Scientific.
Caution: SAVAL Drug-Eluting Vascular Stent System is an investigational device and not available for sale. Ranger DCB is an investigational device and not available for sale in the U.S.

ELUVIA™ DRUG-ELUTING STENT

0.167µg PTX/mm^2 stent surface area

Eluvia™ Drug-Eluting Vascular Stent System

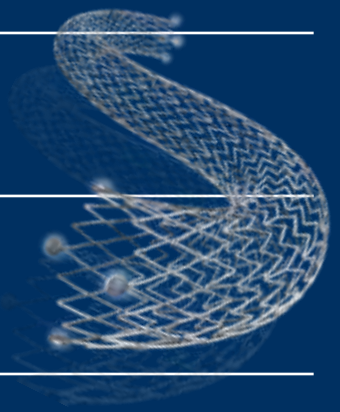
- FDA Approval September 2018
- CE Mark February 2016
- Self-expanding nitinol (Innova stent platform)
- Biostable polymer matrix
- 0.167µg PTX/mm^2 stent surface area



CAUTION: The law restricts these devices to sale by or on the order of a physician. Rx Only.

BSC PI Drug-Eluting Stent Clinical Program

IMPERIAL	**Multicenter, RCT 2:1** (Eluvia : ZilverPTX)	N = 465		1Y follow up complete
MAJESTIC	**Multicenter, single-arm** (Eluvia)	N = 57		3Y follow up complete
EMINENT	**Multicenter, RCT 2:1** (Eluvia : BMS)	N = 750		Enrolling
REGAL	**Multicenter registry** (Eluvia)	N = 500		Enrolling
SPORTS*	**Multicenter, RCT 1:1:1** (Eluvia:DCB:BMS)	N = 222		Enrolling
SAVAL	**Multicenter, RCT 2:1** (DES BTK : PTA) & single-arm	N = 201 & N = 100		Enrolling



*These investigator-sponsored studies are supported by grant funding from Boston Scientific. Boston Scientific is not responsible for the collection, analysis or reporting of these studies which remain the sole responsibility of the investigators. Information for the use in countries with applicable product registrations. SAVAL is an investigational devices and not available for sale in the US.

MAJESTIC Baseline Patient Characteristics (N=57)

Demographics	
Age (Years)	69.3±9.3
Male Gender	82.5%
Race/Ethnicity	
Caucasian	94.7%
Asian	1.8%
Other	3.5%
General Medical History	
Smoking	87.7%
Current Diabetes Mellitus	35.1%
Hyperlipidemia	63.2%
Hypertension	73.7%
Cardiac History	
Coronary Artery Disease	38.6%
Myocardial Infarction (MI)	15.8%
Congestive Heart Failure	5.3%
Peripheral Vascular History	
Peripheral Vascular Surgery	5.3%
Other Peripheral Endovascular Interventions	24.6%
History of Claudication	89.5%

Müller-Hülsbeck S, et al. J Endovasc Ther 2016.

MAJESTIC Summary of Deaths

- All patients treated with Eluvia

CEC-Adjudicated Cause of Death*	3-year Rate
All	3.6% (2/55)
Cardiac	1.8% (1/55)
Vascular	0.0% (0/55)
Non-Cardiovascular	1.8% (1/55)

Site-Reported Cause of Death	CEC Adjudication	Days from Index Procedure
Patient died in nursing home due to cardiac problems	Cardiac Death	368
Complications from metastatic squamous cell carcinoma	Non-cardiovascular Death	652

CEC, Clinical Events Committee.
*The CEC considered all deaths cardiac unless an unequivocal non-cardiac cause could be established.

IMPERIAL Clinical Study Overview

Primary Investigators	Global: William A. Gray, MD European: Stefan Müller-Hülsbeck, MD		
Study Design	**RCT** (Eluvia DES vs Zilver PTX)	**Long Lesion Sub-study** (Eluvia)	**Pharmacokinetic Sub-study** (Eluvia)
	• 2:1 randomized • Single-blind • Non-inferiority trial	• Single arm • Lesion length 140 mm - 190 mm	• Single-arm
Patients	N=465 Eluvia N=309 vs Zilver PTX N=156	N=50	N=13
Investigational Centers	65 study centers: US, Canada, New Zealand, Belgium, Germany, Austria, Japan		

Gray WA, Lancet 2018.

IMPERIAL Baseline Patient Characteristics

	RCT		Long Lesion (N=50)	Pharmacokinetics (N=13)
	Eluvia (N=309)	Zilver PTX (N=156)		
Age (years)	68.5 ± 9.5	67.8 ± 9.4	68.2 ± 8.9	66.4 ± 6.1
Male	66.0%	66.7%	64.0%	76.9%
Smoking status				
Current	35.3%	40.4%	32.0%	23.1%
Previous	50.8%	43.6%	52.0%	76.9%
Diabetes Mellitus	41.7%	43.6%	40.0%	53.8%
Hyperlipidaemia	76.3%	75.6%	82.0%	92.3%
Hypertension	82.2%	85.3%	92.0%	92.3%
Coronary Artery Disease	50.8%	45.2%	56.0%	53.8%
Renal Insufficiency	8.1%	7.1%	6.0%	15.4%

Gray WA, Lancet 2018. Gray WA, VIVA 2018.

IMPERIAL Summary of Deaths: RCT (2:1 randomization)

CEC-Adjudicated Cause of Death*	1-year Rate	
	Eluvia	Zilver PTX
All	2.0% (6/301)	3.9% (6/152)
Cardiac	1.0% (3/301)	3.3% (5/152)
Vascular	0.0% (0/301)	0.7% (1/152)
Non-Cardiovascular	1.0% (3/301)	0.0% (0/152)

Device Type	Site-Reported Cause of Death	CEC Adjudication*	Days from Index Procedure
Eluvia	Cardiac arrest	Cardiac	89
Eluvia	Unknown cause of death	Cardiac	195
Eluvia	Congestive heart failure diastolic dysfunction acute on chronic	Cardiac	275
Eluvia	Multi organ failure	Non-cardiovascular	140
Eluvia	Giant cell B-cell non-Hodgkin lymphoma	Non-cardiovascular	192
Eluvia	Respiratory insufficiency type 1	Non-cardiovascular	329
Zilver PTX	Worsening heart failure	Cardiac	31
Zilver PTX	Cardiac arrest	Cardiac	78
Zilver PTX	Unknown cause of death	Cardiac	171
Zilver PTX	Cardiopulmonary failure	Cardiac	327
Zilver PTX	Coronary heart disease	Cardiac	353
Zilver PTX	Intra-cerebral haemorrhage	Vascular	271

CEC, Clinical Events Committee.
*The CEC considered all deaths cardiac unless an unequivocal non-cardiac cause could be established.

IMPERIAL

Pharmacokinetics (N=13) and Long Lesion (N=50) Sub-studies

- All patients treated with Eluvia
- *Plasma paclitaxel unquantifiable (<1 ng/mL) in 11/13 PK patients at 10 min*, and in all patients at all subsequent timepoints (30 min, and 1, 2, 3, 4, 6, 12, 24, 48 hours post-implant)
- *1-year mortality 0% in both sub-studies*

PK, pharmacokinetics

RANGER DCB

2 µg PTX/mm^2

BSC Peripheral DCB Clinical Program

COMPARE I*	**Multicenter, RCT 1:1** (Ranger : In.Pact)	**N = 414**		Pilot N=150 12M complete. Enrolling extension.
RANGER SFA (FIH)	**Multicenter, RCT 2:1** (Ranger : PTA)	**N = 105**		3Y follow up complete
Ranger SFA Registry*	**Multicenter, registry**	**N = 172**		12M follow up complete
Ranger II Global Pivotal	**Multicenter, RCT 3:1** (Ranger : PTA)	**N = 376**		Enrollment complete
Ranger DCB China	**Multicenter, single-arm**	**N = 123**		Enrolling
RANGER-BTK*	**Single center, single-arm**	**N = 30**		Enrollment complete
DCB vs PTA in CLI and Crural Arteries*	**Single center, RCT 1:1** (Ranger : PTA)	**N = 70**		Enrolling
DCB Venoplasty in AV Fistula Stenosis (DeVA)*	**Multicenter, RCT 1:1** (Ranger : PTA)	**N = 186**		Enrolling

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RANGER SFA Patient Characteristics

	Ranger DCB (N=71)	Control (N=34)	P
Age, y (mean±SD)	68 ± 8	67 ± 9.4	0.999
Men	75%	68%	0.6048
Diabetes mellitus	39%	35%	0.9336
COPD	11%	15%	0.8541
Hyperlipidemia	69%	62%	0.6057
Hypertension	82%	76%	0.6100
Smoking			
Current	41%	50%	0.0217
Previous	45%	21%	
Congestive heart failure	5.6%	2.9%	0.9844
Coronary artery disease	34%	38%	0.8207
Myocardial infarction	14%	15%	1.0000
Cerebrovascular accident	9.9%	2.9%	0.3816
Renal insufficiency	11%	2.9%	0.2920

Bausback Y, et al. J Endovasc Ther. 2017;24(4):459-467.

RANGER SFA Summary of Deaths (2:1 randomization)

CEC-Adjudicated Cause of Death	3-year Rate	
	Ranger DCB	PTA
All	13.8% (9/65)	10.7% (3/28)
Cardiac	4.6% (3/65)	7.1% (2/28)
Vascular	0.0% (0/65)	0.0% (0/28)
Non-Cardiovascular	9.2% (6/65)	3.6% (1/28)

Device Type	Site-Reported Cause of Death	CEC Adjudication	Days from Index Procedure
Ranger DCB	acute heart failure	Cardiac	611
Ranger DCB	acute myocardial infarction	Cardiac	383
Ranger DCB	cardiac decompensation	Cardiac	265
Ranger DCB	worsening of general health and medical history	Non-Cardiovascular	1003
Ranger DCB	pancreas carcinoma	Non-Cardiovascular	477
Ranger DCB	multifactorial diseases	Non-Cardiovascular	859
Ranger DCB	multiple organ failure	Non-Cardiovascular	256
Ranger DCB	carcinoma tonsillaris left	Non-Cardiovascular	843
Ranger DCB	breast cancer	Non-Cardiovascular	450
Control PTA	cardiac decompensation	Cardiac	114
Control PTA	Cardiovascular failure with known coronary artery disease and cardiomyopathy	Cardiac	526
Control PTA	multiorgan failure under hepatorenal syndrome, thrombocytopenia and septic shock	Non-Cardiovascular	397

Conclusions

- Mortality rates with Eluvia were not greater than contemporary rates observed with non-drug-coated devices
  - 2.0% 1-year IMPERIAL vs 2.3% 1-year control[1]
  - 3.6% 3-year MAJESTIC vs 3.8% 2-year control[1]
- 3-year mortality in the randomized RANGER SFA study did not differ between paclitaxel-treated and non-paclitaxel treated arms
- Patient-level data reveals similar causes of death for paclitaxel-treated and non-paclitaxel treated patients

1. Katsanos K, et al. J Am Heart Assoc. 2018 Dec 18;7(24):e011245.